Refine Search

Search Results -

Terms	Documents
il-13ralpha	1

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L8

Refine Search

Recall Text Clear Interrupt

Search History

DATE: Friday, May 27, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=ADJ			
L8	il-13ralpha	1	L8
L7	nr4 receptor	0	L7
L6	il-13 receptor or il-4 receptor	281	L6
L5	antibody with bind with (il-13 or il-4)	54	L5
L4	L1 with antibody	60	L4
L3	L1 same antibody	86	L3
L2	L1 and antibody	260	L2
L1	human il-13 or human il-4	274	L1

END OF SEARCH HISTORY

Refine Search

Search Results -

Terms	Documents
jhang-jian-guo.in.	0

Database: US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: jhang-jian-guo.in.

Refine Search

Recall Text Clear Interrupt

Search History

DATE: Friday, May 27, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L4	jhang-jian-guo.in.	0	L4
L3	hilton-douglas-j.in.	13	L3
L2	nicola-nicos-a.in.	20	L2
L1	wilson-tracy.in.	1	L1

END OF SEARCH HISTORY

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FILE 'MEDLINE' ENTERED AT 10:25:34 ON 27 MAY 2005

FILE 'JAPIO' ENTERED AT 10:25:34 ON 27 MAY 2005
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FILE 'BIOSIS' ENTERED AT 10:25:34 ON 27 MAY 2005
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=> S IL-4 RECEPTOR# OR IL-13 RECEPTOR# OR NR4 OR IL-13RALPHA
   5 FILES SEARCHED...
L1       10263 IL-4 RECEPTOR# OR IL-13 RECEPTOR# OR NR4 OR IL-13RALPHA

=> S IL-4 RECEPTOR# OR IL-13 RECEPTOR#
   5 FILES SEARCHED...
L2        4316 IL-4 RECEPTOR# OR IL-13 RECEPTOR#

=> L2 AND (BIND# IL-4 OR BIND# IL-13)
L3         109 L2 AND (BIND# IL-4 OR BIND# IL-13)

=> DUP REM L3
PROCESSING COMPLETED FOR L3
L4           35 DUP REM L3 (74 DUPLICATES REMOVED)

=> D IBIB ABS L4 1-35

L4   ANSWER 1 OF 35  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER:     2004-143101 [14]   WPIDS
DOC. NO. CPI:         C2004-057703
TITLE:                Identifying compound that modulates interleukin-4 (
                        ***IL***  -  ***4***  )  ***receptor***  -mediated
                      immunoglobulin (IgE) production, comprises determining if
                      compound binds adenosine kinase, useful for treating
                      allergies and atopic disorders.
DERWENT CLASS:        B02 B04 D16
INVENTOR(S):          ANDERSON, D C; BENNETT, M K; KINOSHITA, T; KINSELLA, T M;
                      MASUDA, E; WARNER, J E
PATENT ASSIGNEE(S):   (ANDE-I) ANDERSON D C; (BENN-I) BENNETT M K; (KINO-I)
                      KINOSHITA T; (KINS-I) KINSELLA T M; (MASU-I) MASUDA E;
                      (WARN-I) WARNER J E; (RIGE-N) RIGEL PHARM INC
COUNTRY COUNT:        105
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK      LA   PG
     ---------------------------------------------
     WO 2004007680    A2 20040122 (200414)* EN  124
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
            PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC
            VN YU ZA ZM ZW
     US 2004014147    A1 20040122 (200416)
     AU 2003249218    A1 20040202 (200450)

APPLICATION DETAILS:
```

PATENT NO	KIND	APPLICATION	DATE
WO 2004007680	A2	WO 2003-US21934	20030715
US 2004014147	A1	US 2002-197381	20020716
AU 2003249218	A1	AU 2003-249218	20030715

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003249218	A1 Based on	WO 2004007680

PRIORITY APPLN. INFO: US 2002-197381 20020716
AN 2004-143101 [14] WPIDS
AB WO2004007680 A UPAB: 20040603
NOVELTY - Identifying a compound that modulates interleukin-4 (***IL*** - ***4***) ***receptor*** -mediated immunoglobulin IgE production or a process associated with it, comprising (M1-M2) determining whether the compound binds an adenosine kinase, or contacting a compound from pool of candidate compounds with an adenosine kinase and identifying those compounds of the pool that bind the adenosine kinase, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an AR02E8 compound (C1) comprising a peptide or peptide analog, or its salt, of formula Z1-X1--X2--X3--X4--X5--X6--X7--X8--X9--X10--X11--X12--X13--X14--X15--X16--X17--X18--X19--X20-- X21--X22--X23-Z2 (I), where one or more of X1, X2, X22, or X23 may be absent;

(2) an AR02E8 compound (C2) comprising a peptide or peptide analog of formula Z1-Asp--Thr--Met--Gln--Val--Gln--Cys--Gly--Val --Cys--Arg--Ser-Gly--Tyr--Val--Val--Ala--Phe--Trp--Asp--Val-- Gly--Pro-Z2 (IV), and its variants in which one or two of the amino acid residues set forth in (IV) are replaced by another amino acid selected from the same class as the original amino acid or by an Ala or a Gly residue;

(3) a compound (C3) identified by (M1), where the compound binds adenosine kinase;

(4) a pharmaceutical composition (PC1) comprising (C1) or (C2) and carrier, excipient or diluent;

(5) a pharmaceutical composition (PC2) comprising (C3) and carrier, excipient or diluent;

(6) a kit for identifying compounds that modulate IL-4 induced IgE production, comprising an adenosine kinase or a cell expressing an adenosine kinase and a compound that competitively binds the adenosine kinase in the presence of an active AR02E8 compound; and

(7) treating (M3) an animal suffering from a disease which is caused by, associated with IgE production and/or accumulation and/or symptoms associated with IgE production, by administering a compound which binds adenosine kinase.

X1 = an acidic residue;
X2 = is hydroxyl;
X3 = is a non-polar residue;
X4 = is a polar residue;
X5 = is an aliphatic residue;
X6 = is a polar residue;
X7 = is a cysteine-like residue;
X8 = is an aliphatic residue;
X9 = is an aliphatic residue;
X10 = is cysteine-like residue or an aliphatic residue;
X11 = is a basic residue or an aliphatic residue;
X12 = is a hydroxyl-containing residue, a small polar residue or an aliphatic residue;
X13 = is an aliphatic residue;
X14 = is an aromatic residue;
X15 = is an aliphatic residue;
X16 = is an aliphatic residue;
X17 = is an aliphatic residue;
X18 = is an aromatic residue;
X19 = is an aromatic residue;
X20 = is an acidic residue;
X21 = is an aliphatic residue;
X22 = is an aliphatic residue;
X23 = is a conformationally-constrained residue;

Z1 = is (R)2N-, RC(O)NR-, RS(O)2NR- or an amino-terminal blocking group;

Z2 = is -C(O)OR, -C(O)O-, -C(O)N(R)2 or a carboxyl-terminal blocking group;

R = hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroaryl, heteroarylalkyl and substituted heteroarylalkyl;

-- = an amide, a substituted amide or an isostere of an amide; and

- = represents a bond, or a 1-10 residue peptide or peptide analog;

ACTIVITY - Antiallergic; Dermatological; Antiasthmatic; Antiinflammatory; Ophthalmological; Cytostatic.

No biological data given.

MECHANISM OF ACTION - Inhibitor of IgE production and/or accumulation; Inhibitor IL-4 receptor-mediated signaling cascade; Inhibitor of IL-4 induced switching of B-cells to produce IgE, IL-4 mediated IgE production; Inhibitor of IL-4 induced germline epsilon transcription.

The ability of peptide AR02E8wt to inhibit germline epsilon transcription was tested. Phoenix cells were transfected with a retroviral vector encoding a BFP-AR02E8wt peptide fusion as described in WO 99/58663 and WO 97/27213. Native A5T4 cells were infected with the resultant virions and grown for 3 days. The infected cells were stimulated with interleukin 4 (IL-4) (60 U/ml) and, after 3 days, the cells were assessed by fluorescence activated cell sorting (FACS) for blue fluorescent protein (BFP) and green fluorescent protein (GFP). Infected cells expressed the BFP-peptide fusion (BFP+) and uninfected cells did not express (BFP-). The reporter ratio was determined as the geometric mean of the GFP fluorescence of the BFP- population divided by the geometric mean of the GFP fluorescence of the BFP+ population. The reporter ratio for the AR02E8 in this re-infection assay was 2.93. The ability of peptide AR02E8wt to inhibit transcription of an endogenous germline epsilon promoter was confirmed using a TAQMAN assay. A5T4 cells were infected with retrovirus capable of expressing peptide AR02E8wt. The cells were sorted for BFP+ to select for infected cells. Infected cells were divided into two populations. One population was exposed to Dox (10 ng/ml). Both populations were stimulated with IL-4 (60 U/ml). After 3 days, the cells were pelleted and the pellets assays for epsilon promoter transcription using TAQMAN assay. The primers and probe, which are specific for the transcription product driven by the A5T4 endogenous epsilon promoter, were as follows. epsilon forward primer: ATCCACAGGCACCAAATGGA. epsilon reverse primer: GGAAGACGGATGGGCTCTG. epsilon probe: ACCCGGCGCTTCAGCCTCCA. The measured endogenous epsilon inhibition ratio, defined as the ratio of the relative expression units (TAQMAN quantitative PCR of epsilon transcription product) of +IL-4/+Dox to+IL-4/-Dox cells, was 15.29 indicating that peptide AR02E8wt strongly inhibits the endogenous germline epsilon promoter.

USE - (C1) which binds adenosine kinase, or (C3) which competitively binds adenosine kinase in the presence of active AR02E8 compound, is useful for treating an animal suffering from a disease which is caused by, associated with IgE production and/or accumulation and/or symptoms associated with IgE production. The disease is chosen from allergy (such as anaphylactic allergic reaction), atopic disorder (such as atopic dermatitis, atopic eczema and atopic asthma), allergic rhinitis, allergic conjunctivitis, systemic mastocytosis, hyper IgE syndrome, IgE gammopathies and B-cell lymphoma. (C1) which binds adenosine kinase, or (C3) which competitively binds adenosine kinase in the presence of active AR02E8 compound, is useful for modulating IL-4 (interleukin-4) receptor-mediated IgE production in a cell, where the compound binds adenosine kinase. (C1) which binds adenosine kinase, or (C3) which competitively binds adenosine kinase in the presence of active AR02E8 compound, is useful for inhibiting germline epsilon transcription in a cell, where the compound binds an adenosine kinase (all claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the selection criteria for interaction profiling method used to confirm human adenosine kinase as binding partner for peptide AR02E8wt.

Dwg.8/13

L4 ANSWER 2 OF 35 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1

ACCESSION NUMBER: 2004:714186 SCISEARCH

THE GENUINE ARTICLE: 843UB

TITLE: Gene-gene interaction between interleukin-4 and interleukin-4 receptor alpha in Korean children with asthma

AUTHOR: Lee S G; Kim B S; Kim J H; Lee S Y; Choi S O; Shim J Y; Hong T J; Hong S J (Reprint)

CORPORATE SOURCE: Univ Ulsan, Coll Med, Dept Pediat, 388-1 Poongnap Dong, Seoul 138736, South Korea (Reprint); Univ Ulsan, Coll Med, Dept Pediat, Seoul 138736, South Korea; Univ Ulsan, Asan Inst Life Sci, Seoul, South Korea; Sungkyunkwan Univ, Coll Med, Dept Pediat, Seoul, South Korea; Pusan Natl Univ, Dept Internal Med, Pusan 609735, South Korea

COUNTRY OF AUTHOR: South Korea

SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (AUG 2004) Vol. 34, No. 8, pp. 1202-1208.
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
ISSN: 0954-7894.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 43

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background Interleukin-4 receptor alpha (IL-4Ralpha), which ***binds*** ***IL*** - ***4*** and IL-13, is involved in signal transduction of those cytokines that lead to IgE production, and is also a key functional component of the Th2 lymphocyte phenotype.

Objective To determine whether IL-4 and IL-4Ralpha polymorphisms are associated with susceptibility to asthma and whether there are gene-gene interactions between IL-4 and IL-4Ralpha polymorphisms.

Methods We genotyped three groups of Korean children, consisting of 196 atopic asthmatics, 60 non-atopic asthmatics, and 100 healthy children, for an IL-4 promoter polymorphism (C-590T) and three IL-4Ralpha polymorphisms (Ile50Val, Pro478Ser, and Arg551Gln) using PCR-RFLP (restriction fragment length polymorphism) assays.

Results The allele frequencies of the IL-4 (C/T) polymorphism and the Ile50Val and Pro478Ser polymorphisms of IL-4Ralpha did not differ statistically among the three groups of children. For the Arg551Gln polymorphism, the combined genotype frequency of the Arg/Gln heterozygote and the Arg/Arg homozygote was significantly higher in atopic asthmatics (27.6%) than in healthy children (16.0%) (odds ratio (OR)=1.97, 95% CI (confidence interval)=1.07-3.71). The eosinophil fraction (%) and bronchial responsiveness were higher in children with the Arg/Gln and Arg/Arg genotype than in those with the Gln/Gln genotype (P=0.036 and 0.024, respectively). In asthmatic children, combinations of the IL-4 CT/TT genotype and the IL-4Ralpha Arg/Gln and Arg/Arg genotypes were associated with significantly increased risk for development of asthma (OR=3.70, 95% CI=1.07-12.78, P=0.038).

Conclusions In Korean children, the IL-4Ralpha Arg551 allele may play a role in susceptibility to atopic asthma and correlate with markers of asthma pathogenesis, including increased eosinophil fraction and enhanced bronchial hyper-responsiveness. In addition, a significant gene-gene interaction between the IL-4-590C and the IL-4Ralpha Arg551 allele significantly increases an individual's susceptibility to asthma.

L4 ANSWER 3 OF 35 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004558903 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15531774

TITLE: Therapeutic targeting of IL-4- and IL-13-responsive cells in pulmonary fibrosis.

AUTHOR: Jakubzick Claudia; Kunkel Steven L; Puri Raj K; Hogaboam Cory M

CORPORATE SOURCE: Department of Pathology, University of Michigan Medical School, Ann Arbor, MI 48109, USA.

SOURCE: Immunologic research, (2004) 30 (3) 339-49. Ref: 65
Journal code: 8611087. ISSN: 0257-277X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200504

ENTRY DATE: Entered STN: 20041109
Last Updated on STN: 20050419
Entered Medline: 20050418

AB Severe forms of idiopathic interstitial pneumonia (IIP), such as usual interstitial pneumonia (UIP), can be impervious to modern steroid and immunosuppressive treatment regimens, thereby emphasizing the need for novel effective therapies. Understanding the cytokine networks that may affect immune and structural cell activation and, hence, the progression of these fatal fibrotic diseases, has been a focus in our research. In this regard, we have examined the role of interleukin (IL)-4 and IL-13 and their respective receptor subunits in this process. Examination of clinical surgical lung biopsies (SLBs) showed that IIP is characterized by the abnormal, heightened expression of the receptor subunits that ***bind*** ***IL*** - ***4*** and IL-13. Specifically, IL-4Ralpha and IL-13Ralpha2 (the high-affinity ***IL*** - ***13*** ***receptor*** subunit) was present in greater abundance in SLBs and fibroblasts from IIP patients compared with normal patients, who exhibited no evidence of pulmonary fibrosis. These clinical findings prompted us to investigate whether the targeting of pulmonary cell types that were highly responsive to IL-4 and IL-13 was a viable therapeutic option in IIP. Using a chimeric protein comprised of human IL-13 and a truncated version of an exotoxin from Pseudomonas (abbreviated IL13-PE), we observed that IL13-PE selectively targeted human pulmonary fibroblasts grown from IIP SLBs, whereas it had a minimal effect on fibroblasts grown from biopsies from normal patients. In murine models characterized by abnormal airway or interstitial fibrotic responses, the intranasal administration of IL13-PE significantly attenuated the fibrotic response through the targeting of IL-4Ralpha- and IL-13Ralpha2-expressing pulmonary cells, including monocytes, macrophages, and pulmonary fibroblasts. Together, these data demonstrate that IL-4 and IL-13 are required for the initiation and maintenance of pulmonary fibrosis, and highlight the importance of further investigation of anti-fibrotic therapeutics that prevent the action of both cytokines during clinical pulmonary fibrosis.

L4 ANSWER 4 OF 35 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004095867 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14985454
TITLE: Specifically targeted killing of interleukin-13 (***IL*** - ***13***) ***receptor*** -expressing breast cancer by IL-13 fusion cytotoxin in animal model of human disease.
AUTHOR: Kawakami Koji; Kawakami Mariko; Puri Raj K
CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD, USA.
SOURCE: Molecular cancer therapeutics, (2004 Feb) 3 (2) 137-47. Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20041219
Entered Medline: 20041122

AB Interleukin-13 receptor (IL-13R) alpha2 chain ***binds*** ***IL*** - ***13*** with high affinity and can internalize after binding to ligand. We have exploited this property of IL-13Ralpha2 chain by receptor-targeted breast cancer therapy. Previous studies have demonstrated that in vivo intratumoral (i.t.) gene transfer of this chain followed by IL-13 cytotoxin [comprised of IL-13 and Pseudomonas exotoxin (IL13-PE38QQR)] therapy causes regression of established human tumors in xenografted models. Breast carcinoma cells do not express IL-13Ralpha2 chain and are resistant to the antitumor effect of IL-13 cytotoxin. To determine whether IL-13Ralpha2 chain can render sensitivity of breast cancer to IL-13 cytotoxin, we injected IL-13Ralpha2 plasmid in s.c. established tumors by i.t. route, followed by systemic or i.t. IL-13 cytotoxin administration. This combination approach showed profound antitumor activity against human breast tumors in xenografted immunodeficient mice. Interestingly, there was dominant infiltration of inflammatory cells in regressing tumors, which were identified to be macrophages producing nitric oxide (NO) and natural killer cells. The

partial role of inducible nitric oxide synthase (iNOS)-positive macrophages was confirmed by in vivo macrophage depletion experiments. Serum chemistry, hematology, and organ histology from treated mice did not show any remarkable toxicity resulting from the combination therapy. Taken together, local gene transfer of IL-13Ralpha2 followed by receptor-targeted IL-13 cytotoxin therapy may be applied safely and effectively to the treatment of localized breast cancer.

L4 ANSWER 5 OF 35 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-605377 [57] WPIDS
CROSS REFERENCE: 1990-141470 [19]; 1997-118336 [11]; 1998-144848 [13]; 1998-361747 [31]; 1999-034127 [03]; 1999-105162 [09]; 2002-478536 [51]; 2004-031983 [03]
DOC. NO. CPI: C2003-164714
TITLE: New isolated DNA encoding a soluble IL-4R that binds ILA, fused to a second polypeptide that is not derived from the human IL-4R, useful for suppressing IL-4 mediated immune or inflammatory response.
DERWENT CLASS: B04 D16
INVENTOR(S): BECKMANN, M P; COSMAN, D J; IDZERDA, R; MARCH, C J; MOSLEY, B; PARK, L
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6548655	B1	20030415	(200357)*		47

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6548655	B1	CIP of	US 1988-265047	19881031
		CIP of	US 1989-319438	19890302
		CIP of	US 1989-326156	19890320
		CIP of	US 1989-370924	19890623
		Cont of	US 1990-480694	19900214
		Cont of	US 1998-94917	19980615
			US 2000-724901	20001128

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6548655	B1	Cont of	US 5840869
		Cont of	US 6391581

PRIORITY APPLN. INFO: US 1990-480694 19900214; US 1988-265047 19881031; US 1989-319438 19890302; US 1989-326156 19890320; US 1989-370924 19890623; US 1998-94917 19980615; US 2000-724901 20001128
AN 2003-605377 [57] WPIDS
CR 1990-141470 [19]; 1997-118336 [11]; 1998-144848 [13]; 1998-361747 [31]; 1999-034127 [03]; 1999-105162 [09]; 2002-478536 [51]; 2004-031983 [03]
AB US 6548655 B UPAB: 20040112
NOVELTY - An isolated DNA encoding a soluble IL-4R that binds ILA, fused to a second polypeptide that is not derived from the human IL-4R, comprising 2400 bp, where the soluble human IL-4R comprises amino acids 1-207 or 1-197 of a fully defined sequence of 800 (P1) amino acids, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an expression vector or recombinant expression vector comprising the DNA; and

(2) culturing a suitable host cell comprising the vector under conditions promoting expression of a protein comprising the soluble human IL-4R fused to the polypeptide, and purifying the protein.

USE - The DNA and methods are useful for suppressing IL-4 mediated

immune or inflammatory response. They are also useful in therapy, diagnosis, assay of ***IL*** - ***4*** ***receptors*** , and in raising antibodies to ***IL*** - ***4*** ***receptor*** . Dwg.0/16

L4 ANSWER 6 OF 35 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-164538 [21] WPIDS
CROSS REFERENCE: 1996-476694 [47]; 1998-179442 [16]; 2000-490912 [43]
DOC. NO. NON-CPI: N2002-125575
DOC. NO. CPI: C2002-050852
TITLE: Differentiating brain tumor types and grades by quantifying expression of interleukin-13 receptor in a sample of the tumor and correlating expression of the receptor with tumor type or grade.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): DEBINSKI, W
PATENT ASSIGNEE(S): (PENN-N) PENN STATE RES FOUND; (DEBI-I) DEBINSKI W
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002002799	A1	20020110	(200221)*	EN	25
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
US 2002031492	A1	20020314	(200222)		
AU 2001068744	A	20020114	(200237)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002002799	A1	WO 2001-US20615	20010628
US 2002031492	A1 CIP of	US 1995-404685	19950315
	CIP of	US 1996-706207	19960830
	CIP of	US 1999-226794	19990107
	Provisional	US 2000-215623P	20000630
		US 2001-894609	20010628
AU 2001068744	A	AU 2001-68744	20010628

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2002031492	A1 CIP of	US 5614191
AU 2001068744	A Based on	WO 2002002799

PRIORITY APPLN. INFO: US 2000-215623P 20000630; US 1995-404685 19950315; US 1996-706207 19960830; US 1999-226794 19990107; US 2001-894609 20010628
AN 2002-164538 [21] WPIDS
CR 1996-476694 [47]; 1998-179442 [16]; 2000-490912 [43]
AB WO 200202799 A UPAB: 20021220
NOVELTY - Classifying a brain tumor by type or grade, comprises providing a brain tumor sample, quantifying the expression of an interleukin-13 (***IL*** - ***13***) ***receptor*** in a brain tumor sample and correlating the quantity of expression of ***IL*** - ***13*** ***receptor*** on the sample with tumor type or grade, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for classifying a brain tumor by type and grade, comprising a probe that specifically binds an ***IL*** - ***13*** ***receptor*** and instructions for using the kit to classify a brain tumor by type or grade.
USE - The method is useful for distinguishing a higher-grade brain tumor from a lower-grade brain tumor, where higher expression of

IL - ***13*** ***receptor*** on the sample indicates increased likelihood that the tumor is a high-grade brain tumor and lower expression of ***IL*** - ***13*** ***receptor*** indicates that the tumor is a low-grade brain tumor. The method is also useful for analyzing the prognosis of a subject having a brain tumor, where higher expression of the IL-3 receptor indicates increase likelihood of poor prognosis and lower expression of the IL-3 receptor indicates a decreased likelihood of poor prognosis (all claimed).
Dwg.0/0

L4 ANSWER 7 OF 35 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-478536 [51] WPIDS
CROSS REFERENCE: 1990-141470 [19]; 1997-118336 [11]; 1998-144848 [13]; 1998-361747 [31]; 1999-034127 [03]; 1999-105162 [09]; 2003-605377 [57]; 2004-031983 [03]
DOC. NO. CPI: C2002-136105
TITLE: New nucleic acid encoding interleukin-4 receptor polypeptide, useful for treating e.g. autoimmune and inflammatory diseases, especially soluble receptor forms.
DERWENT CLASS: B04 D16
INVENTOR(S): BECKMANN, M P; COSMAN, D J; IDZERDA, R; MARCH, C J; MOSLEY, B; PARK, L
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6391581	B1	20020521	(200251)*		47

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6391581	B1	CIP of	US 1988-265047	19881031
		CIP of	US 1989-319438	19890302
		CIP of	US 1989-326156	19890320
		CIP of	US 1989-370924	19890623
		Cont of	US 1990-480694	19900214
			US 1998-94917	19980615

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6391581	B1	Cont of	US 5840869

PRIORITY APPLN. INFO: US 1990-480694 19900214; US 1988-265047 19881031; US 1989-319438 19890302; US 1989-326156 19890320; US 1989-370924 19890623; US 1998-94917 19980615
AN 2002-478536 [51] WPIDS
CR 1990-141470 [19]; 1997-118336 [11]; 1998-144848 [13]; 1998-361747 [31]; 1999-034127 [03]; 1999-105162 [09]; 2003-605377 [57]; 2004-031983 [03]
AB US 6391581 B UPAB: 20040112
NOVELTY - New nucleic acid encoding interleukin-4 receptor polypeptide
DETAILED DESCRIPTION - New nucleic acid encoding interleukin-4 receptor polypeptide
The nucleic acid is an isolated DNA (I) encoding a polypeptide (II) that comprises:
(i) amino acids (aa) -25 to 785 or 1-785 of a 810 aa sequence (S2) or aa -25 to 800 or 1-800 of a 825 aa sequence (S4), both defined in the specification, or
(ii) a fragment of (i) that can bind to interleukin-4 (IL-4).
INDEPENDENT CLAIMS are also included for the following:
(1) recombinant expression vector containing (I);
(2) preparation of (II) that ***bind*** ***IL*** - ***4*** by culturing cells that contain the vector of (1);
(3) isolated DNA (Ia) encoding residues -25 to 800, 1-800, -25 to 207

or 1-207 of (S4) in which Ile50 is replaced by Val;
(4) isolated DNA (Ib) encoding a ***IL*** - ***4*** ***receptor*** (IL-4R) polypeptide (IIa) that is at least 80% identical with aa 1-785 or 1-208 of (S2) or aa 1-800 or 1-207 of (S4);
(5) isolated DNA (Ic) encoding a polypeptide (IIb) that differs by one deletion, insertion or substitution from aa 1-785 or 1-208 of (S2) or 1-800 or 1-207 of (S4), and is still able to ***bind*** ***IL*** - ***4*** ;
(6) isolated DNA (Id) encoding a soluble human IL-4R identical to 1-207 of (S4) except for at least one alteration to N-glycosylation sites and/or KEX2 protease processing sites;
(7) isolated DNA (Ie) that is at least 80% identical with nucleotides (nt) -75 to 624 of an approximately 2.4 kb sequence (S2') or to nt -75 to 621 of an approximately 2.45 kb sequence (S4'), defined in the specification;
(8) recombinant expression vector containing any of (Ia)-(Ie);
(9) production of IL-4R polypeptides by culturing cells transformed with the vectors of (8); and
(10) host cells transformed with the vector of (1) where the (II)-encoding unit has integrated into chromosomal DNA.
ACTIVITY - Immunosuppressive; antiallergic; antiarthritic; antirheumatic; antidiabetic; antiinflammatory; dermatological.
When neonatal mouse hearts (H-2b) were transplanted into the pinnae of H-2d recipients, their median survival time was 11.3 days, where the animals had been treated with 100 ng/day murine albumin on days 0, 1 and 2. For animals that also received 1000 ng/day soluble murine IL-4R, mean survival time was 15.3 days.
MECHANISM OF ACTION - (II) ***bind*** ***IL*** - ***4*** , so suppress induction of cytotoxic T cells and, in B cells, proliferation, immunoglobulin secretion and Fc epsilon R expression.
Murine B cells were incubated in presence of affinity-purified goat anti-mouse immunoglobulin M, various concentrations of IL-4 and 1000 ng/ml of soluble IL-4R, then proliferation assessed from incorporation of tritiated thymidine. The soluble receptor inhibited proliferation with half-maximal inhibition at 100-200-fold molar excess of receptor.
USE - (I) encodes the murine or human ***IL*** - ***4*** ***receptor*** (IL-4R), or soluble fragments of it. These fragments are useful for modulating immune and inflammatory responses, e.g. for treating (food) allergy, allergic rhinitis, rheumatoid arthritis, asthma, atopic dermatitis, and diabetes; for preventing allograft rejection and to suppress delayed-type or contact hypersensitivity reactions.
ADVANTAGE - (II) have a very selective immunosuppressive action since they affect only IL-4-mediated responses.
Dwg.0/16

L4 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:51285 CAPLUS
DOCUMENT NUMBER: 136:117387
TITLE: Method for treating cancer using interleukin-4 antagonist
INVENTOR(S): March, Carl J.; Pluenneke, John D.; O'Neal, Larry F.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004009	A2	20020117	WO 2001-US22015	20010711
WO 2002004009	A3	20030821		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,

IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002076409 A1 20020620 US 2001-904245 20010711
PRIORITY APPLN. INFO.: US 2000-217888P P 20000712

AB Methods for treating cancer involve administering an interleukin-4 antagonist to a patient diagnosed with cancer. Suitable IL-4 antagonists include, but are not limited to, ***IL*** - ***4*** ***receptors*** (IL-4R) such as a sol. human ***IL*** - ***4*** ***receptor*** , antibodies that ***bind*** ***IL*** - ***4*** , antibodies that bind IL-4R, IL-4 muteins that bind to IL-4R but do not induce a biol. response, mols. that inhibit IL-4-induced signal transduction, and other compds. that inhibit a biol. effect that results from the binding of IL-4 to a cell surface IL-4R. Co-administration of an IL-4 antagonist and an immune stimulatory mol. is also contemplated. Particular antibodies provided herein include human monoclonal antibodies generated by procedures involving immunization of transgenic mice.

L4 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:11095 CAPLUS
DOCUMENT NUMBER: 136:79758
TITLE: Use of interleukin-4 antagonists and compositions thereof
INVENTOR(S): Pluenneke, John D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp., Cont.-in-part of U.S. Ser. No. 665,343, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002002132	A1	20020103	US 2001-785934	20010215
CA 2409267	AA	20011206	CA 2001-2409267	20010525
WO 2001092340	A2	20011206	WO 2001-US17094	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1283851	A2	20030219	EP 2001-952133	20010525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003124121	A1	20030703	US 2002-324493	20021219

PRIORITY APPLN. INFO.:

US 2000-579808	B2 20000526
US 2000-665343	B2 20000919
US 2001-785934	A 20010215
US 2001-847816	A 20010501
WO 2001-US17094	W 20010525

AB Methods for treating medical conditions induced by interleukin-4 involve administering an IL-4 antagonist to a patient afflicted with such a condition. Suitable IL-4 antagonists include, but are not limited to, ***IL*** - ***4*** ***receptors*** (such as a sol. human ***IL*** - ***4*** ***receptor***), antibodies that ***bind*** ***IL*** - ***4*** , antibodies that bind IL-4R, IL-4 muteins that bind to IL-4R but do not induce a biol. response, mols. that inhibit IL-4-induced signal transduction, and other compds. that inhibit a biol. effect that results from the binding of IL-4 to a cell surface IL-4R. Particular antibodies provided herein include human monoclonal antibodies generated by procedures involving immunization of transgenic mice. Such human antibodies may be raised against human ***IL*** - ***4*** ***receptor*** .

L4 ANSWER 10 OF 35 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002712148 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12354755
TITLE: Kinetic analysis of the interleukin-13 receptor complex.
AUTHOR: Andrews Allison-Lynn; Holloway John W; Puddicombe Sarah M; Holgate Stephen T; Davies Donna E
CORPORATE SOURCE: Infection, Inflammation and Repair Division, School of Medicine, University of Southampton, 97 Tremona Rd., Southampton General Hospital, Southampton SO16 6YD, United Kingdom.
SOURCE: Journal of biological chemistry, (2002 Nov 29) 277 (48) 46073-8. Electronic Publication: 2002-09-26. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030109
Entered Medline: 20030108

AB Interleukin (IL)-13 is a key cytokine associated with the asthmatic phenotype. It signals via its cognate receptor, a complex of ***IL*** - ***13*** ***receptor*** alpha1 chain (IL-13Ralpha1) with IL-4Ralpha; however, a second protein, IL-13Ralpha2, also ***binds*** ***IL*** - ***13*** . To determine the binding contributions of the individual components of the ***IL*** - ***13*** ***receptor*** to IL-13, we have employed surface plasmon resonance and equilibrium binding assays to investigate the ligand binding characteristics of shIL-13Ralpha1, shIL-13Ralpha2, and IL-4Ralpha. shIL-13Ralpha1 bound IL-13 with moderate affinity (K(D) = 37.8 +/- 1.8 nm, n = 10), whereas no binding was observed for hIL-4Ralpha. In contrast, shIL-13Ralpha2 produced a high affinity interaction with IL-13 (K(D) = 2.49 +/- 0.94 nm n = 10). IL-13Ralpha2 exhibited the binding characteristics of a negative regulator with a fast association rate and an exceptional slow dissociation rate. Although IL-13 interacted weakly with IL-4Ralpha on its own (K(D) > 50 microm), the presence of hIL-4Ralpha significantly increased the affinity of shIL-13Ralpha1 for IL-13 but had no effect on the binding affinity of IL-13Ralpha2. Detailed kinetic analyses of the binding properties of the heteromeric complexes suggested a sequential mechanism for the binding of IL-13 to its signaling receptor, in which IL-13 first binds to IL-13Ralpha1 and this then recruits IL-4Ralpha to stabilize a high affinity interaction.

L4 ANSWER 11 OF 35 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002165678 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11786536
TITLE: A novel mechanism by which interferon-gamma can regulate interleukin (IL)-13 responses. Evidence for intracellular stores of ***IL*** - ***13*** ***receptor*** alpha -2 and their rapid mobilization by interferon-gamma.
AUTHOR: Daines Michael O; Hershey Gurjit K Khurana
CORPORATE SOURCE: Division of Allergy and Immunology, Department of Pediatrics, Children's Hospital Medical Center, Cincinnati, Ohio 45229, USA.
CONTRACT NUMBER: P30HD2887 (NICHD)
SOURCE: Journal of biological chemistry, (2002 Mar 22) 277 (12) 10387-93. Electronic Publication: 2002-01-10. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020319
Last Updated on STN: 20030105
Entered Medline: 20020429

AB Interleukin (IL)-13 mediates its activities via a complex receptor system. Interleukin-13 receptor alpha-1 chain (IL-13Ralpha1) ***binds*** ***IL*** - ***13*** with low affinity, but does not signal. However, when IL-13Ralpha1 combines with ***IL*** - ***4*** ***receptor*** alpha (IL-4Ralpha), a signaling high affinity receptor complex for IL-13 is generated. In contrast, IL-13Ralpha2 alone ***binds*** ***IL***

- ***13*** with high affinity, but does not signal and has been postulated to be a decoy receptor. Herein, we investigated the cellular localization of IL-13Ralpha2 and the regulation of its expression by confocal microscopy and flow cytometry in primary and cultured cells. Our results demonstrate that IL-13Ralpha2 is largely an intracellular molecule, which is rapidly mobilized from intracellular stores following treatment with interferon (IFN)-gamma. Up-regulation of IL-13Ralpha2 surface expression in response to IFN-gamma was rapid, did not require protein synthesis, and resulted in diminished IL-13 signaling. These results provide the first evidence that the IL-13Ralpha2 is predominantly an intracellular molecule and demonstrate a novel mechanism by which IFN-gamma can regulate IL-13 responses.

L4 ANSWER 12 OF 35 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002434876 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12192597
TITLE: IL-13Ralpha2 is a glioma-restricted receptor for interleukin-13.
AUTHOR: Mintz Akiva; Gibo Denise M; Slagle-Webb Becky; Christensen Neil D; Debinski Waldemar
CORPORATE SOURCE: Section of Neurosurgery/H110, Pennsylvania State University College of Medicine, 500 University Drive, Hershey, PA 17033-0850, USA.
CONTRACT NUMBER: R01 CA74145 (NCI)
SOURCE: Neoplasia (New York, N.Y.), (2002 Sep-Oct) 4 (5) 388-99. Journal code: 100886622. ISSN: 1522-8002.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020823
Last Updated on STN: 20030221
Entered Medline: 20030220
AB We have found that binding sites for interleukin-13 (IL-13) are overexpressed in a vast majority of high-grade astrocytomas (HGAs). These binding sites for IL-13 are distinct from the physiological receptor in that it does not ***bind*** ***IL*** - ***4*** . We also demonstrated that ***IL*** - ***13*** ***receptor*** alpha 2 protein chain (IL-13Ralpha2), an IL-4-independent receptor for IL-13, is abundant among HGAs, but not in normal organs. To examine if IL-13Ralpha2 is the tumor-associated site for IL-13, we stably transfected normal Chinese hamster ovary (CHO) cells and glioma G-26 cells to express either human (h) or murine (m) IL-13Ralpha2. CHO-hIL-13Ralpha2(+) cells and G-26-h/mIL-13Ralpha2(+) cells, and not CHO and G-26 parental or mock-transfected cells, specifically bound IL-13 in an IL-4-independent manner. The IL-13Ralpha2(+) cells also became highly susceptible to the killing by an IL-13-based cytotoxic fusion protein. In loss of function studies, a HGA cell line, SNB-19, was transfected with antisense (as) hIL-13Ralpha2. as-SNB-19-hIL-13Ralpha2(+) cells lost their natural affinity towards IL-13 and became resistant to IL-13-based cytotoxins. The fact, that IL-13Ralpha2-positive cells ***bind*** ***IL*** - ***13*** independent of IL-4, become susceptible to IL-13 cytotoxins, and cells deprived of IL-13Ralpha2 receptor lose these features, demonstrates that IL-13Ralpha2 is the brain tumor-associated receptor for IL-13.

L4 ANSWER 13 OF 35 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003045067 EMBASE
TITLE: TNF-.alpha. potentiates IL-4/IL-13-induced IL-13R.alpha.2 expression.
AUTHOR: David M.; Bertoglio J.; Pierre J.
CORPORATE SOURCE: J. Pierre, INSERM U461, 5, rue JB Clement, 92296 Chatenay Malabry Cedex, France. josiane.pierre@cep.u-psud.fr
SOURCE: Annals of the New York Academy of Sciences, (2002) Vol. 973, pp. 207-209.
Refs: 4
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030207
Last Updated on STN: 20030207

AB One of the interleukin (***IL***)- ***13*** ***receptor*** chains, the IL-13R.alpha.2, ***binds*** ***IL*** - ***13*** with high affinity, but does not ***bind*** ***IL*** - ***4*** .(3) However, the IL-13/IL-13R.alpha.2 complex was reported to be internalized rapidly, without activating any signaling pathways.(4) Here, we have discussed that tumor necrosis factor (TNF)-.alpha. synergizes with IL-4 and IL-13 in inducing IL-13R.alpha.2 expression in HaCaT cells and is likely to down-regulate the cell responsiveness to IL-13, without affecting IL-4 signaling.

L4 ANSWER 14 OF 35 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002049134 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11741814
TITLE: Effects of IL-13 on airway responses in the guinea pig.
AUTHOR: Morse Brian; Sypek Joseph P; Donaldson Debra D; Haley Kathleen J; Lilly Craig M
CORPORATE SOURCE: Combined Program in Pulmonary and Critical Care Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: KO8 HL-67910 (NHLBI)
RO1 HL/AI-64104 (NHLBI)
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2002 Jan) 282 (1) L44-9.
Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020125
Entered Medline: 20020117

AB Levels of interleukin (IL)-13 are increased in asthmatic airways. IL-13 has been shown to be necessary and sufficient for allergen-induced airway hyperresponsiveness and increased inflammatory cell counts in bronchoalveolar lavage (BAL) fluid in a murine model of asthma but is thought to protect against airway inflammation when low doses are provided to the guinea pig lung. To determine the role of IL-13 in the guinea pig, we studied the effects of a 360-microg/kg dose of nebulized IL-13 in naive animals and of IL-13 abrogation after airway challenge of sensitized animals. Nebulized IL-13 significantly decreased the dose of histamine required to double baseline respiratory system resistance (ED(100), 22 +/- 3 vs. 13 +/- 2 nmol/kg; P < 0.05) and was associated with recovery of significantly greater numbers of macrophages, lymphocytes, eosinophils, and neutrophils in BAL fluid. Guinea pigs pretreated with a fusion protein that ***binds*** ***IL*** - ***13*** [soluble ***IL*** - ***13*** ***receptor*** alpha2 (sIL-13Ralpha2)] were protected from developing antigen-induced airway hyperresponsiveness (ED(100), 210 +/- 50 vs. 20 +/- 10 nmol/kg; P <0.01). sIL-13Ralpha2 (2 doses of 20 mg/kg) significantly reduced the histological grade of allergen-induced lung eosinophil accumulation, whereas the effects of two doses of 10 mg/kg were not significant. These findings demonstrate that the tissue levels of IL-13 induced by allergen challenge of sensitized animals induce airway hyperresponsiveness and inflammation and that IL-13 is required for the expression of allergen-induced airway hyperresponsiveness in the guinea pig ovalbumin model.

L4 ANSWER 15 OF 35 EMBASE
on STN
ACCESSION NUMBER: 2002218091 EMBASE
TITLE: Effects of IL-13 on airway responses in the guinea pig.
AUTHOR: Morse B.; Sypek J.P.; Donaldson D.D.; Haley K.J.; Lilly C.M.
CORPORATE SOURCE: C.M. Lilly, Respiratory Division, Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115, United States. clilly@partners.org

SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2002) Vol. 282, No. 1 26-1, pp. L44-L49.
Refs: 29
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020711
Last Updated on STN: 20020711

AB Levels of interleukin (IL)-13 are increased in asthmatic airways. IL-13 has been shown to be necessary and sufficient for allergen-induced airway hyperresponsiveness and increased inflammatory cell counts in bronchoalveolar lavage (BAL) fluid in a murine model of asthma but is thought to protect against airway inflammation when low doses are provided to the guinea pig lung. To determine the role of IL-13 in the guinea pig, we studied the effects of a 360-.mu.g/kg dose of nebulized IL-13 in naive animals and of IL-13 abrogation after airway challenge of sensitized animals. Nebulized IL-13 significantly decreased the dose of histamine required to double baseline respiratory system resistance (ED(100), 22 .+-. 3 vs. 13 .+-. 2 nmol/kg; P < 0.05) and was associated with recovery of significantly greater numbers of macrophages, lymphocytes, eosinophils, and neutrophils in BAL fluid. Guinea pigs pretreated with a fusion protein that ***binds*** ***IL*** - ***13*** [soluble ***IL*** - ***13*** ***receptor*** .alpha.2 (sIL-13R.alpha.2)] were protected from developing antigen-induced airway hyperresponsiveness (ED(100), 210 .+-. 50 vs. 20 .+-. 10 nmol/kg; P <0.01). sIL-13R.alpha.2 (2 doses of 20 mg/kg) significantly reduced the histological grade of allergen-induced lung eosinophil accumulation, whereas the effects of two doses of 10 mg/kg were not significant. These findings demonstrate that the tissue levels of IL-13 induced by allergen challenge of sensitized animals induce airway hyperresponsiveness and inflammation and that IL-13 is required for the expression of allergen-induced airway hyperresponsiveness in the guinea pig ovalbumin model.

L4 ANSWER 16 OF 35 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-657172 [75] WPIDS
DOC. NO. NON-CPI: N2001-489841
DOC. NO. CPI: C2001-193389
TITLE: Novel isolated canine protein, preferably canine immunoglobulin G protein or canine interleukin-13 receptor protein useful for regulating immune response of an animal and for developing regulatory compounds.
DERWENT CLASS: B04 C06 D16 S03
INVENTOR(S): MCCALL, C A; TANG, L
PATENT ASSIGNEE(S): (HESK-N) HESKA CORP; (MCCA-I) MCCALL C A; (TANG-I) TANG L
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001077332	A2	20011018	(200175)*	EN	221
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001053282	A	20011023	(200213)		
US 2002165135	A1	20021107	(200275)		
EP 1268794	A2	20030102	(200310)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 6703360	B2	20040309	(200418)		
US 2004142372	A1	20040722	(200449)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2001077332	A2		WO 2001-US11498	20010409
AU 2001053282	A		AU 2001-53282	20010409
US 2002165135	A1	Provisional	US 2000-195659P	20000407
		Provisional	US 2000-195874P	20000407
			US 2001-828995	20010409
EP 1268794	A2		EP 2001-926769	20010409
			WO 2001-US11498	20010409
US 6703360	B2	Provisional	US 2000-195659P	20000407
		Provisional	US 2000-195874P	20000407
			US 2001-828995	20010409
US 2004142372	A1	Provisional	US 2000-195659P	20000407
		Provisional	US 2000-195874P	20000407
		Div ex	US 2001-828995	20010409
			US 2004-753159	20040107

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001053282	A	Based on	WO 2001077332
EP 1268794	A2	Based on	WO 2001077332
US 2004142372	A1	Div ex	US 6703360

PRIORITY APPLN. INFO: US 2000-195874P 20000407; US 2000-195659P 20000407; US 2001-828995 20010409; US 2004-753159 20040107

AN 2001-657172 [75] WPIDS

AB WO 200177332 A UPAB: 20011220

NOVELTY - An isolated canine protein (I), preferably canine immunoglobulin G (IgG) protein or canine interleukin-13 (***IL*** - ***13***) ***receptor*** protein, is new.

DETAILED DESCRIPTION - An isolated canine protein (I), preferably canine immunoglobulin G (IgG) protein or canine interleukin-13 (***IL*** - ***13***) ***receptor*** protein, is new. (I) is selected from:

(a) a protein comprising an at least 40 contiguous amino acid region identical in sequence to an at least 40 contiguous amino acid region of a sequence (S1) comprising a 405 residue amino acid fully defined in the specification;

(b) a protein comprising an amino acid sequence that is at least 85 % identical to S1 or its fragment, where the fragment is at least 45 amino acids in length and the percent identity can be determined by a DNAsis (RTM) computer program;

(c) a protein comprising a sequence of at least 30 amino acids in length, where the amino acid sequence has an at least 30 contiguous amino acid region identical in sequence to an at least 30 contiguous amino acid region of a 145, 255, 386, 365 or 318 residue amino acid sequence (S2), fully defined in the specification; and

(d) a protein comprising an amino acid sequence that is at least 70 % identical to S2 or its fragment, where the fragment is at least 40 amino acids in length, and the percent identity is determined by a DNAsis (RTM) computer program.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (II) selected from:

(a) a sequence which has at least 55% identity to a 51 or 60 base pair sequence (S3), both fully defined in the specification, where the identity is determined using a DNAsis (RTM) computer program and default parameters;

(b) a sequence which has at least 95 % identity to a 1654, 1460 or 1456 base pair sequence (S4), all fully defined in the specification;

(c) a sequence which encodes a sequence having at least 40% identity to a 17 or 20 residue amino acid sequence (S5), or 90 % identity to a 468, 17, 470 or 474 residue amino acid sequence (S6), all fully defined in the specification;

(d) a sequence which is an allelic variant of S3, S4 or a 473 residue amino acid sequence (S7), fully defined in the specification; and

(e) a complement of (a)-(e);

(2) an isolated nucleic acid molecule (III) selected from:

(a) a sequence comprising at least 70, or 350 contiguous nucleotides of S3 or S4, respectively;

(b) a sequence comprising at least 450 contiguous nucleotides of a sequence comprising a 1453 base pair sequence, fully defined in the specification;

(c) a sequence which encodes an amino acid sequence comprising at least 20, 100 or 200 contiguous residues of S5, S6 or S7, respectively; and

(d) a sequence complementary to (a)-(c);

(3) a recombinant vector (IV) comprising (II) or (III);

(4) a fusion construct (V) comprising (II) or (III);

(5) a recombinant cell (VI) comprising (II) or (III);

(6) an isolated antibody (VIII) selective for (VII);

(7) an isolated cell (IX) comprising (VII);

(8) an isolated fusion protein (X) comprising (VII);

(9) detecting (M1) IgG nucleic acid involves contacting (II) with a putative IgG nucleic acid-containing composition under conditions suitable for formation of a heavy chain of canine IgG nucleic acid molecule/IgG nucleic acid complex, and detecting the presence of IgG nucleic acid by detecting the heavy chain of canine IgG nucleic acid molecule/IgG nucleic acid complex;

(10) a kit (XI) comprising a container which comprises at least one composition selected from (II) or (III), (VII), an inhibitor of (II) or (III), and an inhibitor of (VII);

(11) an isolated nucleic acid molecule (XII) selected from:

(a) a nucleic acid molecule comprising at least 75 contiguous nucleotides identical in sequence to an at least 75 contiguous nucleotide region of a 483, 1547 or 1215 base pair sequence (S8), all fully defined in the specification; and

(b) a nucleic acid molecule comprising a sequence that is at least 90 % identical to S8, or its fragment, where the fragment is at least 80 nucleotides in length, and the percent identity is determined by a DNAsis (RTM) computer program with a gap penalty set at 5, the number of top diagonals set at 5, a fixed gap penalty set at 10, a k-tuple set at 2, a window size set at 10 and a floating gap penalty set at 10;

(12) an isolated nucleic acid molecule (XIII) selected from:

(a) a nucleic acid molecule having at least 40 contiguous nucleotides identical in sequence to at least 40 contiguous nucleotide region of a 620, 878, 1454, 1158, 1095 or 954 base pair sequence (S9), all fully defined in the specification; and

(b) a nucleic acid molecule comprising a nucleic acid sequence that is at least 80 % identical to S9 or its fragment, where the fragment is at least 50 nucleotides in length, and the percent identity is determined by a DNAsis (RTM) computer program with a gap penalty set at 5, the number of top diagonals set at 5, a fixed gap penalty set at 10, a k-tuple set at 2, a window size set at 10 and a floating gap penalty set at 10;

(13) a chimeric nucleic acid molecule (XVI) encoding a fusion protein comprising a nucleic acid molecule encoding a carrier protein domain, and a nucleic acid molecule encoding a canine IL-13R alpha -protein domain;

(14) a recombinant molecule (XVII) comprising (XVI);

(15) a recombinant virus or cell comprising (XII), (XIV), (XV) or (XVI);

(16) a fusion protein (XX) comprising a carrier protein domain, and a canine IL-13 receptor alpha (IL-13 R alpha) protein domain;

(17) an isolated antibody (XXI) that selectively binds to (I), (II) or (XX);

(18) production of (I);

(19) identifying (M2) a compound that inhibits the activity of a canine IL-13R alpha protein, comprising contacting an isolated canine IL-13R alpha protein with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-13R alpha protein has IL-13 binding activity, and determining if the inhibitory compound inhibits the activity; and

(20) an assay kit (XXIII) to identify an inhibitor of canine IL-13R alpha protein, comprises an isolated canine IL-13R alpha protein, and a unit for determining inhibition of an activity of canine IL-13R alpha , where the unit enables the detection of inhibition, and the detection of inhibition identifies an inhibitor of the ability of the canine IL-13R alpha protein to bind IL-13.

ACTIVITY - Immunosuppressive.
MECHANISM OF ACTION - Regulator of immune response. Regulator of IL-13 activity; gene therapy.
No biological data is given.
USE - (XXII) is useful for regulating an immune response in a canine (claimed). (I) is useful to develop regulatory compounds including inhibitors and activators that, when administered to a canine in an effective manner, are capable of protecting canine from disease mediated by IL-13R alpha or IL-13. (XXII) is useful for treating canine IgG (heavy and/or light chain) and/or canine IL-13R mediated responses. (I), (II), (III), (VII), (XII), (XV), (XXI) or (XXII) is useful to regulate the immune response of an animal.
Dwg.0/0

L4 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:886250 CAPLUS
DOCUMENT NUMBER: 136:36357
TITLE: Use of interleukin-4 antagonists and compositions thereof
INVENTOR(S): Pluenneke, John D.
PATENT ASSIGNEE(S): Immunex Corp., USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092340	A2	20011206	WO 2001-US17094	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002002132	A1	20020103	US 2001-785934	20010215
CA 2409267	AA	20011206	CA 2001-2409267	20010525
EP 1283851	A2	20030219	EP 2001-952133	20010525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:		
US 2000-579808	A	20000526
US 2000-665343	A	20000919
US 2001-785934	A	20010215
US 2001-847816	A	20010501
WO 2001-US17094	W	20010525

AB Methods for treating medical conditions induced by interleukin-4 involve administering an IL-4 antagonist to a patient afflicted with such a condition. Suitable IL-4 antagonists include, but are not limited to, ***IL*** - ***4*** ***receptors*** (such as a sol. human ***IL*** - ***4*** ***receptor***), antibodies that ***bind*** ***IL*** - ***4*** , antibodies that bind IL-4R, IL-4 muteins that bind to IL-4R but do not induce a biol. response, mols. that inhibit IL-4-induced signal transduction, and other compds. that inhibit a biol. effect that results from the binding of IL-4 to a cell surface IL-4R. Particular antibodies provided herein include human monoclonal antibodies generated by procedures involving immunization of transgenic mice. Such human antibodies may be raised against human ***IL*** - ***4*** ***receptor*** . Certain of the antibodies inhibit both IL-4-induced and IL-13-induced biol. activities. Also discussed is a sol. interleukin 4 receptor as an antagonist. These antagonists can be used to treat septic arthritis.

L4 ANSWER 18 OF 35 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001376717 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11352909
TITLE: Identification of distinct roles for a dileucine and a

tyrosine internalization motif in the interleukin (IL)-13 binding component ***IL*** - ***13*** ***receptor*** alpha 2 chain.
AUTHOR: Kawakami K; Takeshita F; Puri R K
CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD 20892, USA.
SOURCE: Journal of biological chemistry, (2001 Jul 6) 276 (27) 25114-20. Electronic Publication: 2001-05-14. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20030105
Entered Medline: 20010809

AB Interleukin (***IL***)- ***13*** ***receptor*** alpha2 (IL-13Ralpha2) chain is an essential binding component for IL-13-mediated ligand binding. Recently, we have demonstrated that this receptor chain also plays an important role in the internalization of IL-13. To study the mechanism of IL-13 internalization, we generated mutated IL-13Ralpha2 chains that targeted trileucine residues (Leu(335), Leu(336), and Leu(337)) in the transmembrane domain and a tyrosine motif (Tyr(343)) in the intracellular domain and transfected these cDNAs in COS-7 cells. Cells that expressed a C-terminally truncated IL-13Ralpha2 chain (Delta335) did not ***bind*** ***IL*** - ***13*** , suggesting that the trileucine region modulates IL-13 binding. Truncation of IL-13Ralpha2 chain with a mutation in the trileucine region resulted in significantly decreased internalization compared with wild type IL-13Ralpha2 chain transfected cells. COS-7 cells transfected with tyrosine motif mutants exhibited a similar internalization level compared with wild type IL-13Ralpha2 chain transfected cells; however, dissociation of cell surface IL-13 was faster compared with wild type IL-13Ralpha2 transfectants. These results were further confirmed by determining the cytotoxicity of a chimeric protein composed of IL-13 and a mutated form of Pseudomonas exotoxin (IL13-PE38QQR) to cells that expressed IL-13Ralpha2 chain mutants. We further demonstrate that the IL-13Ralpha2 chain is not ubiquitinated and that internalization of IL-13Ralpha2 did not depend on ubiquitination. Together, our findings suggest that the dileucine motif in the trileucine region and tyrosine motif participate in IL-13Ralpha2 internalization in distinct manners.

L4 ANSWER 19 OF 35 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2001662232 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11709700
TITLE: Induction of the ***IL*** - ***13*** ***receptor*** alpha2-chain by IL-4 and IL-13 in human keratinocytes: involvement of STAT6, ERK and p38 MAPK pathways.
AUTHOR: David M; Ford D; Bertoglio J; Maizel A L; Pierre J
CORPORATE SOURCE: INSERM U461, Faculte de Pharmacie, 5, rue JB Clement, 92296 Chatenay Malabry Cedex, France.
SOURCE: Oncogene, (2001 Oct 11) 20 (46) 6660-8. Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011119
Last Updated on STN: 20020123
Entered Medline: 20011207

AB IL-4 and IL-13 are related cytokines which induce both pro- and anti-inflammatory effects depending on the cell type they act upon and the nature of the receptors expressed. The type I receptor complex is composed of the IL-4Ralpha and gammac and only ***binds*** ***IL*** - ***4*** , whereas, in the type II receptor, IL-4Ralpha dimerizes with IL-13Ralpha1 upon either IL-4 or IL-13 binding. Another ligand binding chain potentially implicated in the IL-4/ ***IL*** - ***13***

receptor has been described, the IL-13Ralpha2, but the regulation of its expression and its role in IL-4/IL-13 transduction is poorly understood. In this study we report that IL-4 and IL-13 upregulate IL-13Ralpha2 at both the mRNA and protein levels in the keratinocyte cell line HaCaT. In these cells, IL-4 or IL-13 were shown to activate the Janus Kinases JAK1 and JAK2, the transcription factor STAT6, and the ERK and p38 mitogen-activated protein kinases. We show that IL-4 or IL-13-induced IL-13Ralpha2 mRNA expression was inhibited by the ERK inhibitor U0126, the JAK inhibitor AG490 and, to a lesser extent, the p38 MAPK inhibitor SB203580. Moreover, expression of a constitutive active mutant of STAT6 alone did not modify IL-13Ralpha2 mRNA expression, but potentiated the effects of IL-4 or IL-13 on IL-13Ralpha2 expression. The constitutive active mutants of MEK1 or MKK6 increased the level of expression of IL-13Ralpha2 mRNA even in absence of stimulation. Our findings demonstrate, for the first time, that IL-4 and IL-13 can induce IL-13Ralpha2 expression in keratinocytes, and that the ERK and p38 MAPK together with JAK2 and STAT6 play a critical role in this process.

L4 ANSWER 20 OF 35 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001340848 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11313257
TITLE: The interleukin-13 receptor alpha2 chain: an essential component for binding and internalization but not for interleukin-13-induced signal transduction through the STAT6 pathway.
AUTHOR: Kawakami K; Taguchi J; Murata T; Puri R K
CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Blood, (2001 May 1) 97 (9) 2673-9.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB The interleukin-13 receptor (IL-13R) complex is composed of 2 different chains, IL-13Ralpha1 (also known as IL-13Ralpha') and IL-13Ralpha2 (also known as IL-13Ralpha). For a functional ***IL*** - ***13*** ***receptor*** , the IL-13Ralpha1 chain forms a productive complex with the primary IL-4 binding protein (IL-4Ralpha also known as IL-4Rbeta). However, the function of the IL-13Ralpha2 chain is not clear even though this chain ***binds*** ***IL*** - ***13*** with high affinity. This study demonstrates that IL-13Ralpha2 can undergo internalization after binding to ligand without causing activation of its signaling pathways. These conclusions were drawn on the basis of (1) internalization of (125)I-IL-13 in Chinese hamster ovarian (CHO-K1) and T98G glioblastoma cells transiently transfected with the IL-13Ralpha2 chain; (2) a recombinant chimeric fusion protein comprising IL-13 and a mutated form of Pseudomonas exotoxin (termed IL13-PE38QQR or IL-13 toxin) is specifically cytotoxic to IL-13Ralpha2-transfected CHO-K1 cells in a gene dose-dependent manner, whereas cells transfected with vector alone were not sensitive; and (3) IL-13 did not cause activation of signal transduction and activation of transcription 6 (STAT6) in IL-13Ralpha2-transfected cells. IL-13 efficiently caused activation of STAT6 protein in cells transfected with the IL-13Ralpha1 and IL-4Ralpha chains, and IL-13Ralpha2 inhibited this activation. Taken together, these observations indicate that internalization of IL-13Ralpha2 is signal independent and that this property of IL-13Ralpha2 can be exploited for receptor-directed cancer therapy.

L4 ANSWER 21 OF 35 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001212283 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11160216
TITLE: Reconstitution of a functional human type II IL-4/ ***IL*** - ***13*** ***receptor*** in mouse B cells: demonstration of species specificity.

AUTHOR: Andrews R; Rosa L; Daines M; Khurana Hershey G
CORPORATE SOURCE: Division of Pulmonary Medicine, Allergy, and Clinical Immunology, Department of Pediatrics, Children's Hospital Medical Center, Cincinnati, OH 45229, USA.
CONTRACT NUMBER: P30HD2887 (NICHD)
RO1A146652-01A1
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2001 Feb 1) 166 (3) 1716-22.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

AB IL-13 is a Th2-derived pleiotropic cytokine that recently was shown to be a key mediator of allergic asthma. IL-13 mediates its effects via a complex receptor system, which includes the IL-4R alpha-chain, IL-4Ralpha, and at least two other cell surface proteins, IL-13Ralpha1 and IL-13Ralpha2, which specifically ***bind*** ***IL*** - ***13*** . IL-13 has been reported to have very limited effects on mouse B cells. It was unclear whether this was due to a lack of receptor expression, a disproportionate relative expression of the receptor components, or an additional subunit requirement in B cells. To determine the requirements for IL-13 signaling in murine B cells, we examined IL-13-dependent Stat6 activation and CD23 induction in the murine B cell line, A201.1. A201.1 cells responded to murine IL-4 via the type I IL-4R, but were unresponsive to IL-13, and did not express ***IL*** - ***13*** ***receptor*** . B220(+) splenocytes also failed to signal in response to IL-13 and did not express ***IL*** - ***13*** ***receptor*** . We transfected A201.1 cells with human IL-4Ralpha, IL-13Ralpha1, or both. Transfectants expressing either human IL-4Ralpha or human IL-13Ralpha1 alone were unable to respond or signal to IL-13. Thus, human IL-13Ralpha1 could not combine with the endogenous murine IL-4Ralpha to generate a functional IL-13R. However, cells transfected with both human IL-4Ralpha and IL-13Ralpha1 responded to IL-13. Thus, the relative lack of IL-13 responsiveness in murine B cells is due to a lack of receptor expression. Furthermore, the heterodimeric interaction between IL-4Ralpha and IL-13Ralpha1 is species specific.

L4 ANSWER 22 OF 35 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 12
ACCESSION NUMBER: 2001:821925 SCISEARCH
THE GENUINE ARTICLE: 481CY
TITLE: Expression of a functional IL-13R alpha 1 by rat B cells
AUTHOR: Pierrot C; Beniguel L; Begue A; Khalife J (Reprint)
CORPORATE SOURCE: Inst Pasteur, INSERM, Unite 547, IFR 17, 1 Rue Prof Calmette, F-59019 Lille, France (Reprint); Inst Pasteur, INSERM, Unite 547, IFR 17, F-59019 Lille, France; Inst Biol Lille, CNRS 1160, F-59019 Lille, France
COUNTRY OF AUTHOR: France
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (5 OCT 2001) Vol. 287, No. 4, pp. 969-976.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 0006-291X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 46

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB IL-13 mediates its effects through a complex receptor system including IL-4R alpha and a functional IL-13R alpha1. IL-13 has been reported to have no effects on mouse B cells due to a lack of receptor expression. However, on human B cells a functional IL-13R alpha1 has been described. Here, we identified the rat IL-13R alpha1 in order to analyze its expression and function in rat B cells. The expression of IL-13R alpha1 has been shown by the presence of mRNA and the corresponding protein in purified rat B cells and in rat hybridoma B cell line. Rat B cells are able to ***bind*** ***IL*** - ***13*** and to proliferate when

cultured with CD40 ligand and IL-13. In vivo experiments showed that administration of IL-13 did enhance IgE production. These results suggest a direct interaction of rat B cells with IL-13 through a functional receptor with an increase of IgE production and provide a relevant model to further study the activity of IL-13 and to better understand its role in human diseases. (C) 2001 Academic Press.

L4 ANSWER 23 OF 35 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1998256353 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9593769
TITLE: Interleukin (IL) 4 and IL-13 act on human lung fibroblasts. Implication in asthma.
AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clemenceau C; Canonica G W; Jasmin C; Azzarone B
CORPORATE SOURCE: U268 INSERM Hopital Paul Brousse, 94807 Villejuif Cedex, France.
SOURCE: Journal of clinical investigation, (1998 May 15) 101 (10) 2129-39.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980619

AB Airway hyperresponsiveness leading to subepithelial fibrosis is mediated by inflammatory cells activated by T helper (Th) 2-derived cytokines such as IL-4 and IL-5. By analyzing the phenotype and response of human lung fibroblasts derived from either fetal (ICIG7) or adult (CCL202) tissue as well as from a Th2-type stromal reaction (FPA) to IL-4 and IL-13, we provide evidence that human lung fibroblasts may behave as inflammatory cells upon activation by IL-4 and IL-13. We show that the three types of fibroblasts constitute different populations that display a distinct pattern in cell surface molecule expression and proinflammatory cytokine and chemokine release. All fibroblasts express functional but different IL-4/ ***IL*** - ***13*** ***receptors*** . Thus, while ***IL*** - ***4*** ***receptor*** (R) alpha and IL-13Ralpha1 chains are present in all the cells, CCL202 and FPA fibroblasts coexpress the IL-13Ralpha2 and the IL-2Rgamma chain, respectively, suggesting the existence of a heterotrimeric receptor (IL-4Ralpha/IL-13Ralpha/IL-2Rgamma) able to ***bind*** ***IL*** - ***4*** and IL-13. Stimulation with IL-4 or IL-13 triggers in the fibroblasts a differential signal transduction and upregulation in the expression of beta1 integrin and vascular cell adhesion molecule 1 and in the production of IL-6 and monocyte chemoattractant protein 1, two inflammatory cytokines important in the pathogenesis of allergic inflammation. Our results suggest that when activated by IL-4 and IL-13, different subsets of lung fibroblasts may act as effector cells not only in the pathogenesis of asthma but also in lung remodeling processes. They may also differentially contribute to trigger and maintain the recruitment, homing, and activation of inflammatory cells.

L4 ANSWER 24 OF 35 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1998447468 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9776573
TITLE: Detection of and discrimination between total and free human interleukin-4 and free soluble interleukin-4 receptor by ELISA.
AUTHOR: Jung T; Bews J P; Enssle K H; Wagner K; Neumann C; Heusser C H
CORPORATE SOURCE: Department of Dermatology, University Gottingen, Germany.
SOURCE: Journal of immunological methods, (1998 Aug 1) 217 (1-2) 41-50.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810

ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981027

AB Interleukin-4 (IL-4) signaling is initiated by binding of IL-4 to the high-affinity ***IL*** - ***4*** ***receptor*** alpha-chain and subsequent interaction with the common gamma-chain. Soluble forms of the extracellular domain of the alpha-chain (sIL-4R) were shown to be present in biological fluids and, dependent on the concentration, enhance or inhibit IL-4 activity by forming IL-4/sIL-4R complexes. To discriminate between free and potentially active IL-4 from the inactive and complexed form, we have established a set of new ELISA systems for the measurement of human IL-4 in its distinct forms. To select suitable pairs of anti-IL-4 antibodies, a chequerboard interference analysis with six highly-selective human IL-4 specific monoclonal antibodies was performed. For the determination of total IL-4, a monoclonal capture antibody was used that ***binds*** ***IL*** - ***4*** outside the binding site of the IL-4R alpha-chain. Another antibody recognizing an epitope of the alpha-chain binding site was chosen for the detection of free IL-4. The binding of this antibody was inhibited in a dose-dependent fashion by recombinant sIL-4R. Assays for both total and free IL-4 exhibited a sensitivity of 8 pg/ml and a dynamic range up to 1000 pg/ml. Human sIL-4R was detected by two monoclonal antibodies directed against different epitopes. This ELISA was inhibited by recombinant IL-4 suggesting the measurement of predominantly free sIL-4R. Complexes between soluble IL-4R and IL-4 were detected by a monoclonal anti-sIL-4R antibody in combination with an anti-IL-4 antibody. When supernatants of activated T cells were analyzed, the majority of the IL-4 was in free form. The amount of complexed IL-4 was low as indicated by the fact that most of total IL-4 could be detected as free IL-4. Although values obtained for complexed IL-4 correlated with the difference between total and free IL-4, precise values could not be determined, presumably due to the dynamic nature of the complex between the two proteins. We suggest that the ability to quantitate total and free IL-4 in combination with sIL-4R may provide a new insight of the role that IL-4 plays in different pathophysiological conditions.

L4 ANSWER 25 OF 35 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 97238889 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9083087
TITLE: Identification, purification, and characterization of a soluble interleukin (IL)-13-binding protein. Evidence that it is distinct from the cloned ***Il*** - ***13*** ***receptor*** and ***Il*** - ***4*** ***receptor*** alpha-chains.
AUTHOR: Zhang J G; Hilton D J; Willson T A; McFarlane C; Roberts B A; Moritz R L; Simpson R J; Alexander W S; Metcalf D; Nicola N A
CORPORATE SOURCE: Walter and Eliza Hall Institute of Medical Research and the Cooperative Research Centre for Cellular Growth Factors, P.O. Royal Melbourne Hospital, Victoria 3050, Australia.
SOURCE: Journal of biological chemistry, (1997 Apr 4) 272 (14) 9474-80.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 20000303
Entered Medline: 19970508

AB Interleukin-4 (IL-4) and interleukin-13 (IL-13) are structurally and functionally related cytokines which play an important role in the regulation of the immune response to infection. The functional similarity of IL-4 and IL-13 can be explained, at least in part, by the common components that form their cell surface receptors, namely the ***IL*** - ***4*** ***receptor*** alpha-chain (IL-4Ralpha) and the ***IL*** - ***13*** ***receptor*** alpha-chain (IL-13Ralpha). Soluble forms of the IL-4Ralpha have also been described and implicated in modulating the effect of IL-4. In this paper we describe the presence of a 45,000-50,000 Mr IL-13-binding protein (IL-13BP) in the serum and urine

of mice. This protein ***binds*** ***IL*** - ***13*** with a 100-300-fold higher affinity (KD = 20-90 pM) than does the cloned IL-13Ralpha (KD = 3-10 nM). In addition to this functional difference, the IL-13BP appears to be structurally and antigenically distinct from the IL-13Ralpha. Finally, unlike the cloned receptor, the IL-13BP acts as a potent inhibitor of IL-13 binding to its cell surface receptor, raising the possibility that it may be used to modulate the effects of IL-13 in vivo.

L4 ANSWER 26 OF 35 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 97146045 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8992992
TITLE: The ***IL*** - ***13*** ***receptor*** structure differs on various cell types and may share more than one component with ***IL*** - ***4*** ***receptor***.
AUTHOR: Obiri N I; Leland P; Murata T; Debinski W; Puri R K
CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Food and Drug Administration, Center for Biologics Evaluation and Research, Bethesda, MD 20892, USA.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1997 Jan 15) 158 (2) 756-64.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 20020420
Entered Medline: 19970211

AB We have reported on the expression and characteristics of IL-13R and have demonstrated that IL-13 competes for IL-4 binding while IL-4 did not compete for the IL-13 binding on some cell types. Based on these observations, and the size of IL-13 and IL-4 cross-linked proteins, we concluded that the receptor for IL-13 is complex and shares a subunit with the receptor for IL-4. To explore the complexity of the IL-13R, a wide variety of cell types was examined for IL-13 and IL-4 binding. We report in this work that IL-4 does not always bind well to cells that ***bind*** ***IL*** - ***13*** , but the reverse is also true. We also found that IL-4 can compete more effectively for IL-13 binding than IL-13 itself. Cross-linking studies support these observations and demonstrate that 125I-labeled IL-13 bound exclusively to a single 65- to 70-kDa protein in MA-RCC and U251 cells, while in TF-1 cells it cross-linked to two membrane proteins of 65 to 70 kDa and 140 kDa. Furthermore, by using a chimeric protein composed of IL-13 and Pseudomonas exotoxin A, we observed that IL-4 neutralized the cytotoxicity of the IL-13 toxin on COS-7 cells by blocking a common form of the two cytokine receptors. We propose that the 65- to 70-kDa form of the IL-13R is the predominant common component shared between IL-13 and IL-4R. However, the primary IL-4 binding (p140) protein also participates in the formation of the IL-13R complex in some cell types. In addition, the gamma(c) or another interactive subunit may influence IL-13 binding to its receptor complex. Thus, we propose that there are at least four forms of IL-13R.

L4 ANSWER 27 OF 35 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 97165986 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9013879
TITLE: Cloning of the human IL-13R alpha1 chain and reconstitution with the IL4R alpha of a functional IL-4/ ***IL*** - ***13*** ***receptor*** complex.
AUTHOR: Miloux B; Laurent P; Bonnin O; Lupker J; Caput D; Vita N; Ferrara P
CORPORATE SOURCE: Sanofi Recherche, Labege Innopole, France.
SOURCE: FEBS letters, (1997 Jan 20) 401 (2-3) 163-6.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y09328

ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19980206
Entered Medline: 19970227

AB The human homologue of the recently cloned murine IL-13 binding protein (IL-13R alpha1) was cloned from a cDNA library derived from the carcinoma cell line CAKI-1. The cloned cDNA encodes a 427 amino acid protein with two consensus patterns characteristic of the hematopoietic cytokine receptor family and a short cytoplasmic tail. The human protein is 74% identical to the murine IL-13R alpha1, and 27% identical to the human IL-13R alpha2. CHO cells expressing recombinant hIL-13R alpha1 specifically ***bind*** ***IL*** - ***13*** (Kd approximately 4 nM) but not IL-4. Co-expression of the cloned cDNA with that of IL-4R alpha resulted in a receptor complex that displayed high affinity for IL-13 (Kd approximately 30 pM), and that allowed cross-competition of IL-13 and IL-4. Electrophoretic mobility shift assay showed that IL-13 and IL-4 were able to activate Stat6 in cells expressing both IL-4R alpha and IL-13R alpha1, while no activation was observed in cells expressing either one or the other alone.

L4 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:214782 CAPLUS
DOCUMENT NUMBER: 124:281083
TITLE: Identifying agents that bind the interleukin 4 signal transducer and transcription activator for potential therapeutic use
INVENTOR(S): Mcknight, Steven L.; Hou, Jinzhao
PATENT ASSIGNEE(S): Tularik, Inc., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 692488	A2	19960117	EP 1995-304715	19950705
EP 692488	A3	19990317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5591825	A	19970107	US 1994-276099	19940715
PRIORITY APPLN. INFO.:			US 1994-269604 A	19940705
			US 1994-276099 A	19940715

AB Methods and compns. for identifying pharmacol. agents useful in the diagnosis or treatment of disease assocd. with the expression of a gene modulated by an interleukin 4 signal transducer and activator of transcription, IL-4 Stat, are described. IL-4 Stat peptides and ***IL*** - ***4*** ***receptor*** peptides and nucleic acids encoding such peptides find therapeutic uses. The peptides may inhibit IL-4 Stat binding to the receptor or to their DNA binding site. The subject compns. include IL-4 Stat and ***IL*** - ***4*** ***receptor*** proteins, portions thereof, nucleic acids encoding them, and specific antibodies. The disclosed pharmaceutical screening methods are particularly suited to high-throughput screening where one or more steps are performed by a computer controlled electromech. robot comprising an axial rotatable arm. Purifn. of IL-4 Stat and demonstration of inhibition by ***IL*** - ***4*** ***receptor*** peptides is demonstrated. Receptor peptides that ***bind*** ***IL*** - ***4*** Stat prevent formation of the active dimer form.

L4 ANSWER 29 OF 35 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 96279273 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8663118
TITLE: Cloning and characterization of a specific interleukin (IL)-13 binding protein structurally related to the IL-5 receptor alpha chain.
AUTHOR: Caput D; Laurent P; Kaghad M; Lelias J M; Lefort S; Vita N; Ferrara P
CORPORATE SOURCE: Sanofi Recherche, BP 137, 31676 Labege Cedex, France.
SOURCE: Journal of biological chemistry, (1996 Jul 12) 271 (28) 16921-6.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X95302
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960911
Last Updated on STN: 19980206
Entered Medline: 19960829

AB Interleukin-13 (IL-13) is a cytokine secreted by activated T lymphocytes that shares many, but not all, biological activities with IL-4. These overlapping activities are probably due to the existence of common receptor components. Two proteins have been described as constituents of the ***IL*** - ***4*** ***receptor*** , a approximately 140-kDa glycoprotein (IL-4R) and the gamma chain (gammac) of the IL-2 receptor, but neither of these proteins ***binds*** ***IL*** - ***13*** . We have cloned a cDNA encoding an IL-13 binding protein (IL-13R) from the Caki-1 human renal carcinoma cell line. The cloned cDNA encodes a 380-amino acid protein with two consensus patterns characteristic of the hematopoietic cytokine receptor family and a short cytoplasmic tail. The IL-13R shows homology with the IL-5 receptor, and to a lesser extent, with the prolactin receptor. COS-7 cells transfected with the IL-13R cDNA ***bind*** ***IL*** - ***13*** with high affinity but do not ***bind*** ***IL*** - ***4*** . COS-7 cells co-transfected with the cloned IL-13R cDNA and IL-4R cDNA resulted in the reconstitution of a small number of receptors that recognized both IL-4 and IL-13. Reverse transcription-polymerase chain reaction analysis detected the receptor transcript only in cell lines known to ***bind*** ***IL*** - ***13*** .

L4 ANSWER 30 OF 35 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 95275171 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7755507
TITLE: Soluble ***IL*** - ***4*** ***receptor*** , potential for therapeutic and prophylactic intervention.
AUTHOR: Gessner A; Rollinghoff M
CORPORATE SOURCE: Institute for Clinical Microbiology and Immunology, University of Erlangen-Nurnberg, Germany.
SOURCE: Behring Institute Mitteilungen, (1994 Dec) (95) 35-41. Ref: 23
Journal code: 0367532. ISSN: 0301-0457.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19980206
Entered Medline: 19950620

AB Many bacterial, protozoal and viral infections trigger a cell-mediated immune response. Of special importance for the clinical outcome of disease, however, is the relative predominance of T helper (Th) cell populations (Th1 and Th2) secreting different patterns of lymphokines. Preferential development of one Th subset occurs apparent at the early stages of an infection, suggesting that the mechanisms driving the immune response in one direction or the other operate soon after exposure to the antigen. Cytokines are among the most important factors regulating T cell differentiation and expansion of the different T cell subtypes. As in experimental candidiasis, listeriosis, yersiniosis and murine retrovirus induced immunodeficiency syndrome (MAIDS), interleukin-4 (IL-4) is of central importance also for the clinical course of murine cutaneous leishmaniasis. It has been demonstrated that the presence of IL-4 is essential for the development of disease promoting Th2 cells whereas neutralization of IL-4 in vivo led to establishment of protective immunity against leishmania. A naturally occurring antagonist of IL-4 is the soluble ***IL*** - ***4*** ***receptor*** (sIL-4R), which retains its ligand binding properties and ***binds*** ***IL*** - ***4*** with high affinity. We therefore examined the immunomodulatory

and therapeutic capacity of recombinant sIL-4R in murine cutaneous leishmaniasis. BALB/c mice were treated with recombinant sIL-4+ during the onset of the immune response. This treatment rendered BALB/c mice clinically resistant to Leishmania major (L. major), led to reduced parasite load, shifted the pattern of cytokines towards Th1 type and provided durable resistance against reinfection with L. major.(ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 31 OF 35 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 94183392 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7907877
TITLE: Interleukin 13, an interleukin 4-like cytokine that acts on monocytes and B cells, but not on T cells.
AUTHOR: Zurawski G; de Vries J E
CORPORATE SOURCE: Dept of Molecular Biology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104.
SOURCE: Immunology today, (1994 Jan) 15 (1) 19-26. Ref: 45
Journal code: 8008346. ISSN: 0167-5699.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940509
Last Updated on STN: 19950206
Entered Medline: 19940426
AB Interleukin 13 (IL-13) is a recently described protein secreted by activated T cells which is a potent in vitro modulator of human monocyte and B-cell functions. The data, reviewed here by Gerard Zurawski and Jan de Vries, shows that IL-13 shares biological activities with IL-4, their genes are closely linked in both the human and mouse genomes, and there is sequence homology between IL-13 and IL-4 proteins. Although the cloned ***IL*** - ***4*** ***receptor*** protein (IL-4R) does not ***bind*** ***IL*** - ***13*** , it appears that the functional IL-4R and IL-13R share a common subunit that is important for signal transduction.

L4 ANSWER 32 OF 35 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1991-339758 [46] WPIDS
DOC. NO. CPI: C1992-025813
TITLE: Isolated and purified Interleukin-4 binding protein-gamma - used to inhibit interleukin-4-mediated immune responses e.g. IGE-induced immediate hypersensitivity and T-cell function.
DERWENT CLASS: B04 D16
INVENTOR(S): ARMITAGE, R J; FANSLOW, W C
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9116348	A	19911031	(199146)*		
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE					
W: AU CA JP KR					
AU 9178597	A	19911111	(199207)		
EP 528928	A1	19930303	(199309)	EN	35
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
US 5223605	A	19930629	(199327)		13
EP 528928	B1	19961009	(199645)	EN	22
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
DE 69122612	E	19961114	(199651)		
ES 2095319	T3	19970216	(199714)		
IE 75902	B	19971008	(199749)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 528928	A1	EP 1991-909599	19910329

			WO 1991-US2227	19910329
US 5223605	A	CIP of	US 1990-509672	19900416
			US 1990-598489	19901016
EP 528928	B1		EP 1991-909599	19910329
			WO 1991-US2227	19910329
DE 69122612	E		DE 1991-622612	19910329
			EP 1991-909599	19910329
			WO 1991-US2227	19910329
ES 2095319	T3		EP 1991-909599	19910329
IE 75902	B		IE 1991-1109	19910403

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 528928	A1	Based on	WO 9116348
EP 528928	B1	Based on	WO 9116348
DE 69122612	E	Based on	EP 528928
		Based on	WO 9116348
ES 2095319	T3	Based on	EP 528928

PRIORITY APPLN. INFO: US 1990-509672 19900416; US 1990-598489 19901016

AN 1991-339758 [46] WPIDS

AB WO 9116348 A UPAB: 19930928

An isolated and purified Interleukin-4 Binding Protein-gamma (IL-4b gamma) compsn. is new.

Also claimed is a process for prepg. an isolated and purified IL-4b gamma) compsn. comprising: (a) applying a non-homogeneous sample contg. IL-4b gamma to an affinity matrix comprising an IL-4 or anti-IL-4b gamma antibody molecule bound to an insoluble support; and (b) eluting the IL-4b gamma. Further claimed are antibodies immunoreactive with mammalian IL-4b gamma.

Specifically the IL-4b gamma is a glycoprotein having an N-terminal amino acid (AA) sequence of

Thr-Ser-Pro-Gln-Gln -Pro-Ala-Ala-Arg-Pro Ser-Asp-Leu-Leu-Ser Leu-Asp-Gly-Ser

It has an apparent mol.wt. of 45-50 kD (SDS-PAGE).

USE - The IL-4b gamma is an IL-4 antagonist and can be used for inhibiting IL-4-mediated immune responses. It can be used to inhibit IgE antibody formation in the treatment of IL-4-mediated IgE-induced immediate hypersensitivity reactions such as allergic rhinitis, bronchial asthma, atopic dermatitis and gastrointestinal food allergy. It can also be used to regulate IL-4-mediated T-cell functions, e.g. to treat allograft rejection or graft-versus-host reactions or to treat autoimmune dysfunctions such as rheumatoid arthritis or diabetes. The IL-4b gamma can also be used as an immunogen, a reagent in immunoassays or as a binding agent for affinity purification of IL-4 or other binding ligands. (Previously notified in week 9146)

0/0

ABEQ US 5223605 A UPAB: 19931116

Isolated an purified IL-4 binding protein-gamma comprises the N-terminal aminoacid sequence Thr-Ser-Pro-Gln-Gln-Pro-Ala-Ala -Arg-Pro-Ser-Asp-Leu-Leu-Ser-Leu -Asp-Gly-Ser, and ***binds*** ***IL*** - ***4*** and inhibits IL-4 bonding to a cell surface receptor. Protein is of human origin (e.g. from JM-1 cells), is preferably a glycoprotein and has a mol. wt. of 45-50 kD by SDS-PAGE.

USE/ADVANTAGE - For therapy, diagnosis, assays of IL-4bp-gamma, IL-4 or ***IL*** - ***4*** ***receptors*** and for raising antibodies to IL-4bp-gamma.

Dwg.0/1

ABEQ EP 528928 B UPAB: 19961111

An isolated and purified Interleukin-4 Binding Protein-gamma comprising an N-terminal amino acid sequence of ThrSerProGlnGlnProAlaAlaArgProSerAspLeuLeuSerLeuAspGlySer, that is capable of binding to Interleukin-4 and inhibiting binding of Interleukin-4 to a cell surface receptor.

Dwg.0/1

L4 ANSWER 33 OF 35 MEDLINE on STN DUPLICATE 21

ACCESSION NUMBER: 91284192 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2060018

TITLE: Evaluation of murine interleukin 4 (***IL*** - ***4***) ***receptor*** expression using anti-receptor monoclonal antibodies and S1 nuclease protection analyses.
AUTHOR: Ishida H; Yang G; Harada N; Hastings R L; Castle B E; Kastelein R; Miyajima A; Howard M
CORPORATE SOURCE: DNAX Research Institute of Molecular and Cellular Biology, Incorporated, Palo Alto, California 94304.
SOURCE: Cellular immunology, (1991 Aug) 136 (1) 142-54. Journal code: 1246405. ISSN: 0008-8749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910825
Last Updated on STN: 19980206
Entered Medline: 19910808

AB Anti-receptor antibodies have previously been used in two cytokine systems (IL-1 and TNF alpha) to identify the existence of different cytokine receptors on different cell types. In this study, we have similarly used two approaches to evaluate whether ***IL*** - ***4*** ***receptors*** on different cell types are identical, or whether more than one species of ***IL*** - ***4*** ***receptor*** exists. The first approach involved production of monoclonal antibodies specific for the ***IL*** - ***4*** ***receptor*** expressed by the murine mast cell line, MC/9. Six anti- ***IL*** - ***4*** ***receptor*** monoclonal antibodies were produced against the purified soluble extracellular domain of the recombinant ***IL*** - ***4*** ***receptor*** derived from MC/9 cells. These antibodies were capable of binding to and specifically immunoprecipitating the soluble extracellular domain of the recombinant mast cell ***IL*** - ***4*** ***receptor*** . Following biotinylation of the antibodies and addition of phycoerythrin-streptavidin, their binding to cell associated ***IL*** - ***4*** ***receptors*** on MC/9 mast cells could be readily visualized by immunofluorescence. Using this approach, the anti-mast cell IL-4R antibodies were found to specifically ***bind*** ***IL*** - ***4*** ***receptors*** expressed on a variety of other murine cell types, including T cells, B cells, macrophages, fibroblasts, and L cells. The antibodies did not bind to two human cell lines known to bind human but not murine IL-4. The intensity of staining was directly related to the number of IL-4 binding sites identified previously by receptor-ligand equilibrium binding analyses. As a second approach to evaluating potential receptor heterogeneity, we constructed S1 nuclease protection assay probes for two separate regions of the mast cell ***IL*** - ***4*** ***receptor*** , one located in the extracellular domain and one in the intracellular domain. Subsequent S1 analyses showed that both regions are expressed by the following types of cells: T cells, B cells, macrophages, myeloid cells, L cells, and stromal cells. The two approaches used in this study therefore indicate that the same or highly similar ***IL*** - ***4*** ***receptor*** species is expressed by a wide variety of hemopoietic and nonhemopoietic cells. Since the anti- ***IL*** - ***4*** ***receptor*** antibodies produced in this study did not block binding of IL-4 to its receptor, we cannot exclude the possible existence of a second type of IL-4R coexpressed on the cells tested in this study, or expressed uniquely by other cell types that were not investigated.

L4 ANSWER 34 OF 35 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 90272682 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2349230
TITLE: A soluble, high-affinity, interleukin-4-binding protein is present in the biological fluids of mice.
AUTHOR: Fernandez-Botran R; Vitetta E S
CORPORATE SOURCE: Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235.
CONTRACT NUMBER: AI-11851 (NIAID)
AI-21229 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1990 Jun) 87 (11) 4202-6. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900810
Last Updated on STN: 19900810
Entered Medline: 19900712

AB Cytokines such as interleukin 4 (IL-4) play a key role in the regulation of immune responses, but little is known about how their multiple activities are regulated in vivo. In this report, we demonstrated that an IL-4-binding protein (IL-4BP) is constitutively present in the biological fluids of mice (serum, ascites, fluid, and urine). Binding of 125I-labeled IL-4 to the IL-4BP is specific and saturable and can be inhibited by an excess of unlabeled IL-4 but not IL-2. The IL-4BP ***binds*** ***IL*** - ***4*** with an affinity similar to that reported for the cellular ***IL*** - ***4*** ***receptor*** (Kd approximately 7 x 10(-11) M) and has a molecular mass of 30-40 kDa and pI values of 3.6-4.8. IL-4BP-containing biological fluids or purified IL-4BP competitively inhibit the binding of 125I-labeled IL-4 to mouse T or B cells and inhibit the biological activity of IL-4 but not IL-2. The serum levels of IL-4BP in severe combined immunodeficiency (SCID) mice are lower than those of normal mice. The above findings suggest that IL-4BP plays an important immunoregulatory role in vivo.

L4 ANSWER 35 OF 35 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 91370704 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2104233
TITLE: A soluble form of the interleukin 4 receptor in biological fluids.
AUTHOR: Fanslow W C; Clifford K; VandenBos T; Teel A; Armitage R J; Beckmann M P
CORPORATE SOURCE: Immunex Corporation, Seattle, Washington 98101.
SOURCE: Cytokine, (1990 Nov) 2 (6) 398-401.
Journal code: 9005353. ISSN: 1043-4666.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911108
Last Updated on STN: 19980206
Entered Medline: 19911018

AB Murine biological fluids and murine cell culture supernatants were analyzed for the presence of soluble murine interleukin 4 receptor (sIL4R) with the use of two monoclonal antibodies directed against the receptor. Mouse urine, serum, ascitic fluid, and cell culture supernatants contained varying levels of immunoreactive protein. All of the immunoreactive protein possessed interleukin 4 (IL 4) binding activity. Following partial purification of ascitic fluid a protein was isolated that ***binds*** ***IL*** ***4*** with high affinity. This data is consistent with the fact that murine biological fluids contain a soluble version of the murine ***IL*** ***4*** ***receptor*** that arises via secretion of the soluble receptor and/or via shedding of the extracellular portion of the full-length receptor from the cell surface.